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The Doppler profile of ovarian endometrioma

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Abstract

Aims. *To characterize the vascularity of endometriotic cysts using color Doppler ultrasound and to differentiate more accurately between endometriotic cysts and other pelvic cyst masses.* ***Methods.*** *Two prospective studies were initiated: the first included 50 patients diagnosed with ovarian endometriotic cysts and 50 patients without gynecological pathology, in whom the resistance index (RI) of the uterine artery, ovarian artery and endometrial arcuate arteries in the early secretory phase was determined by endovaginal Doppler ultrasound; the second study included 50 patients diagnosed with ovarian endometriotic cysts, in whom the RI of the uterine artery, ovarian artery and cyst wall arteries in the late proliferative phase and in the late secretory phase was determined.* ***Results.*** *In the early secretory phase, the vascular flow through the uterine artery was significantly higher in patients with ovarian endometrioma. These patients had increased endometrial vascularity in the early secretory phase compared to the control group. In the late secretory phase, the vascular flow through the ovarian artery was higher compared to the late proliferative phase in patients with ovarian endometrioma. The vascularization of the ovarian endometrioma wall was significantly increased in the late secretory phase compared to the late proliferative phase.* ***Conclusions.*** *Vascularization, described through the arrangement of vessels, vascular density and vascular resistance, is an important factor in the evaluation of ovarian endometrioma.*
Keywords: *Doppler, endometriotic cysts, vascular flow*

Introduction

Endometriosis is a chronic estrogen-dependent inflammatory disease, which involves the presence of functional endometrial glands and stroma outside the uterine cavity.

Between 20% and 50% of all women treated for infertility have endometriosis[(1)], while up to 80% of women with chronic pelvic pain can be affected by this pathological condition[(2)].

The pathogenesis of this disease is unclear, involving genetic, endocrine, immune and environmental factors. Recently, studies of genetic association have emphasized correlations between the development of endometriosis and certain genetic polymorphisms, even though the genes that are involved in the susceptibility to the development and progression of endometriosis are still unknown[(3)].

The ovary is a frequent site of ectopic endometrial tissue. Ovarian endometrioma is characterized by 2D ultrasound as having a polyhedral outline, a thick wall, homogeneous fine echogenic content, being frequently unilocular, often with echogenic wall inclusions - old hematic pigments.

However, these elements are not pathognomonic for ovarian endometrioma, as they can also be ultrasonographically detected in the corpus luteum, intracystic hemorrhage, dysgerminoma, thecoma, dermoid cyst, ovarian abscess. Doppler ultrasound can provide additional information to clarify these aspects of differential diagnosis[(4)].

The aim of this study was to characterize the vascularity of endometriotic cysts using Doppler ultrasound.

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Methods

In order to determine the Doppler profile of ovarian endometrioma, two prospective studies were initiated. The first, a case-control study, included 50 patients diagnosed with ovarian endometriosis cysts and 50 patients without gynecological pathology, in whom the following parameters were assessed by endovaginal Doppler ultrasound: the resistance index (RI) of the uterine artery, ovarian artery and endometrial arcuate arteries, in the early secretory phase (days 17-18 of the menstrual cycle). There were no significant differences between the two groups regarding the age, menarche and body mass index. The second study, a representative sample one, included 50 patients diagnosed with ovarian endometriotic cysts, in whom the following parameters were determined: the RI of the uterine artery, ovarian artery and cyst wall arteries, at two different times of the menstrual cycle, in the late proliferative phase (days 12-13 of the cycle), and in the late secretory phase (days 24-25 of the cycle). The second study contained the same 50 patients with endometrioma included in the first case group. Ultrasound was performed with a Voluson 730 machine equipped with a 5 MHz vaginal probe.

The patients with endometriomas were included in the study based on the following criteria: diagnosis of ovarian endometrioma ≥4cm, supported by 2D ultrasound followed by surgery (laparoscopy-laparotomy), with histopathological examination confirming endometriosis. The exclusion criteria were: current hormonal treatment, presence of uterine fibroma, imaging signs of adenomyosis, gynecological malformations,

autoimmune diseases, chronic diseases, coagulation disorders, and previous surgery for endometriosis, other previous gynecological surgeries or inflammatory pelvic disease.

A detailed medical, gynecological and obstetric history of the patients was obtained at their inclusion in the study. After the morphological assessment of the adnexal mass by 2D ultrasound, color Doppler ultrasound was used to map vascularization, and pulsed Doppler to determine RI at the evaluated sites. At least four correctly visualized consecutive blood flow velocity wave forms were analyzed for the calculation of RI.

All patients with endometriomas ≥4cm were operated: laparoscopy was carried out under general anesthesia, while laparotomy was performed under rachianesthesia or general anesthesia, depending on the case. Excision by enucleation of unilateral or bilateral endometriomas was conducted by experienced surgeons.

The informed consent of all patients was obtained. The study was conducted under the tenets of the Helsinki Declaration.

Statistical Analysis

From a statistical point of view, in the case of the comparison of two means for independent samples, the Student test or the Mann-Whitney test was used for the comparison of the ranks. In the case of the comparison of two means for dependent samples, the Student test for paired samples or the Wilcoxon test was used. Normal distribution was assessed using the Kolmogorov-Smirnov test. Correlation was calculated via the Pearson or the Spearman correlation coefficient, the latter being used in the case of the presence of aberrant values.

Results

The characteristics of the patients are described in Table 1.

The RI of the uterine artery showed a significantly lower value ($p<0.001$) in the case group0.80±001 (with a range between 0.79 and 0.84), compared to the control group 0.88±001 (with a range between 0.86 and 0.91), in the early secretory phase. Thus, in this phase, the vascular flow in the uterine artery was increased in patients with ovarian endometrioma (Figure 2).

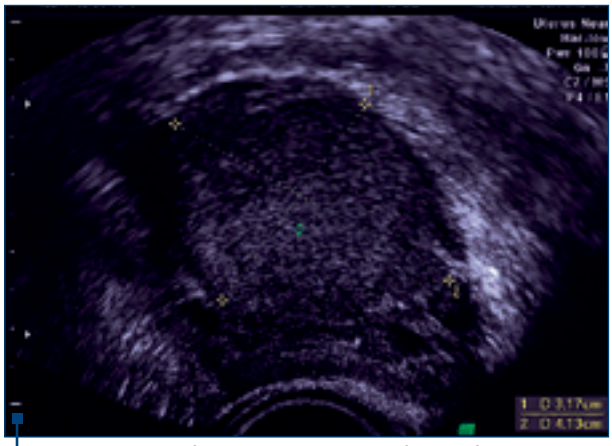

Figure 1. Ovarian endometrioma aspecct in 2D ultrasound

Ovarian artery resistance was significantly higher ($p<0.001$) in the control group, 0.76±002 (with a range between 0.69 and 0.79), compared to the case group, 0.61±002 (with a range between 0.58 and 0.65), in the early secretory phase (Figure 3). The vascularization of ovarian endometrioma, derived from the ovarian artery, was significantly increased compared to the vascularization of the normal ovary in the early secretory phase (Figure 4).

The RI of the arcuate arteries was significantly higher ($p<0.001$) in the control group,0.58±001 (with a range between 0.55 and 0.59), compared to the case group (patients with ovarian endometrioma), 0.50±001 (with a range between 0.48 and 0.54), in the early secretory phase. Patients with ovarian endometrioma showed an increased endometrial vascularization in the early secretory phase compared to healthy women (Figure 5).

Patients with ovarian endometrioma had a significantly higher uterine artery resistance ($p<0.001$) in the

Table 1 Characteristics of the patients included in the study

Characteristics of patients	Control (n=50 patients)		Cases (n=50 patients)		p
	Mean±SD	Range	Mean±SD	Range	
Age	35.55±3.04	25-59	34.12±2.08	24-58	NS
Menarche	12.02±0.46	11-14	12.38±0.16	11-14	NS
BMI	21.34±1.31	18.4-25.5	22.41±2.04	18.7-26.1	NS
Cyst diameter	-	-	6.36±0.43		

Note: 95%=95% Confidence Interval for Mean; SD=Standard Deviation; NS=nesignificant; BMI= body mass index.

late proliferative phase, 0.87±003 (with a range between 0.78 and 0.94), compared to the late secretory phase, 0.80±0.01 (with a range between 0.79 and 0.84). Thus, the vascularization of ovarian endometrioma derived from the uterine artery was significantly increased in the late secretory phase (Figure 6).

The RI of the ovarian artery had a significantly higher value ($p<0.001$) in the late proliferative phase, 0.85±002 (with a range between 0.78 and 0.87), compared to the late secretory phase, 0.61±002 (with a range between 0.58 and 0.65), in patients with ovarian endometrioma. Thus, in the late secretory phase, the vascular flow through the ovarian artery was higher compared to the late proliferative phase in patients with ovarian endometrioma (Figure 7).

Vascular resistance in the endometriotic cyst wall arteries was significantly higher ($p<0.001$) in the late proliferative phase, 0.71±003 (with a range betwe-en0.63 and 0.79), compared to the late secretory phase, 0.52±002 (with a range between 0.49 and 0.58). The vascularization of the ovarian endometrioma wall was significantly increased in the late secretory phase compared to the late proliferative phase (Figure 8 and Table 2).

Discussion

The most frequent ultrasound appearance of ovarian endometrioma is hypoechogenic, "frosted glass". The homogeneous filling of the cyst with low-level echoes has been considered a useful sign in the detection of endometriotic cysts. However, this ultrasonographic aspect of endometriosis cysts does not seem to be pathognomonic. This pattern was identified by Aleemet et al.[5] in only 38% of the cases. Sometimes, an endometriotic cyst may contain diffuse low-reflection areas or may acquire a solid ultrasound appearance. A very old cyst can become completely anechogenic, with posterior enhancement[6].

Ultrasound examination can detect a change in the echogenicity of the endometrioma during the menstrual phase of the menstrual cycle, when intracystic bleeding causes the development of a multitude of interfaces between old blood and fresh blood areas, which confer a loculated appearance.

Doppler ultrasound evidences in the case of endometriotic cysts vascularity aspects that place these entities in the category of benign ovarian tumors: peripheral vascularization, high maximum systolic velocity (MSV) (normal 20-60 cm/sec), increased blood flow resistance (pulsatility index =1-1.5), presence of the protodiastolic notch[7]. These vascular characteristics can also be detected in the case of other ovarian tumors: serous cystadenoma, mucinous cystadenoma, dermoid cyst, mesenchymal tumors.

The aim of this study was to characterize the vascularity of endometriotic cysts using color Doppler ultrasound. Doppler signals might contribute to the differentiation of these cysts from other ovarian tumors or other pelvic pathology.

The majority of studies reported that endometriosis cysts do not appear as vascular cysts, although these data are in disagreement with those of Timor-Tritsch[8], who evidenced the presence of blood flow in 71% of endometriotic cysts, assessed by color Doppler ultrasound.

Luteal cysts are characterized by peripheral vascularization, low RI, a thick and highly vascularized wall[9].

Ovarian neoplasms are clearly differentiated from endometriosis cysts through the 2D ultrasound appearance and particularly, through the characteristics of vascularization: abundant, with central location, dense vascular distribution, low resistance, high MSV. The percentage of positive diagnosis of malignant ovarian tumors with low resistance is 90-95%[7]. An important element in making diagnosis is the pulsatility index, whose value lower than 1 is an important indicator of malignancy[10]. However, 1/3 of all operated ovarian tumors suspected of malignancy prove to be benign on histo-pathological examination[11]. As tumor vessels are newly formed vessels, their wall thickness does not contain the muscular component, the wall being formed only by the adventitia and intima, which is why spectral characteristics include: high diastolic flow with low resistance ($RI<0.75$, $PI<1$), absence of the protodiastolic notch. Tumor vessels have an irregular tract, they show multiple arteriovenous shunts and are grouped in amorphous tumor pools[12].

The Doppler characteristics of follicular cysts include: peripheral vascularization, presence of the protodiastolic notch, low RI (recently formed cyst), moderate/high RI (old cyst), respectively. These aspects do not show essential differences compared to ovarian endometrioma. The differentiation from endometriosis cyst consists of the lack of variation in vascularity depending on the menstrual cycle phases. Luteal cysts occurring after ovarian stimulation treatment are characterized by peripheral vascularization, absence of the protodiastolic notch, low RI[13].

Serous cystadenoma as well as mucinous cystadenoma have the following vascular characteristics: reduced vascularization with peripheral location, presence of the protodiastolic notch, high resistance. These vascular aspects are similar to those of endometrioma[14]. Unlike in the case of endometrioma, cyst wall artery resistance does not vary depending on the menstrual cycle phases.

In the case of dermoid cyst, central vascularization is absent, while peripheral vascularization characterized by a moderate/high RI can be detected, which could allow differentiation from endometrioma[15]. Even if the presence of the protodiastolic notch does not contribute to the differentiation of endometrioma from the dermoid cyst, the variation of resistance with menstruation can be a differentiation element.

Unlike endometrioma, thecoma shows on Doppler evaluation vessels of regular caliber both at the periphery and in the central area, as well as low resistance[16]. The ultrasonographic pattern of dysgerminoma is similar to that of other malignant ovarian tumors: dense, irregular, tortuous vessels of large caliber, wi-

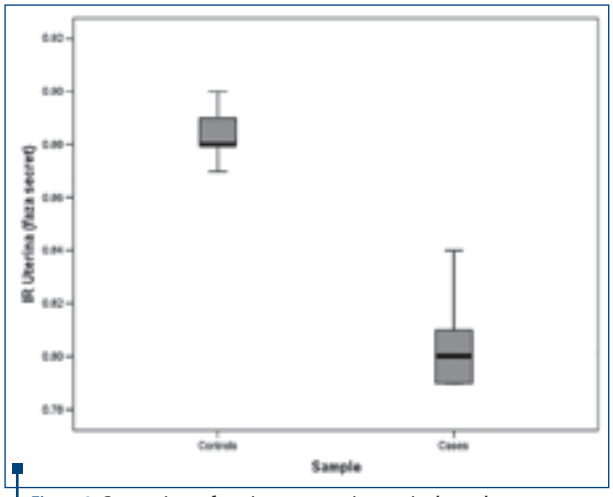

Figure 2. Comparison of uterine artery resistance in the early secretory phase

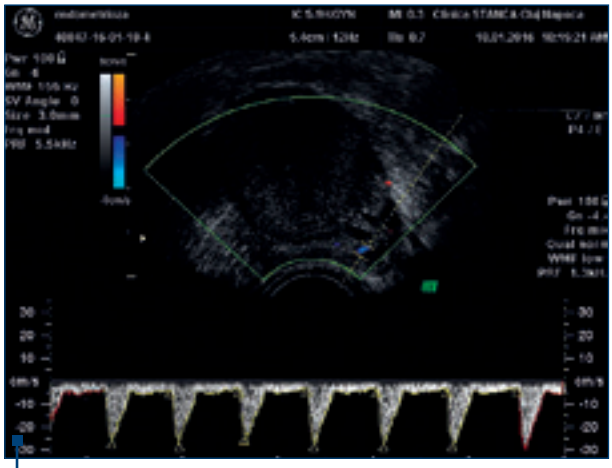

Figure 3. Ovarian artery resistance

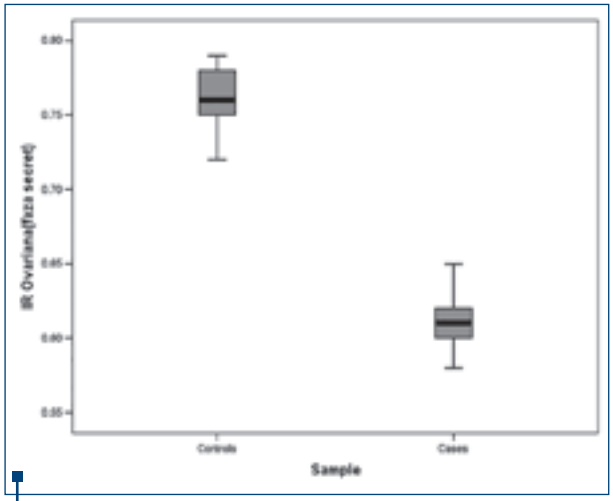

Figure 4. Comparison of ovarian artery resistance in the early secretory phase

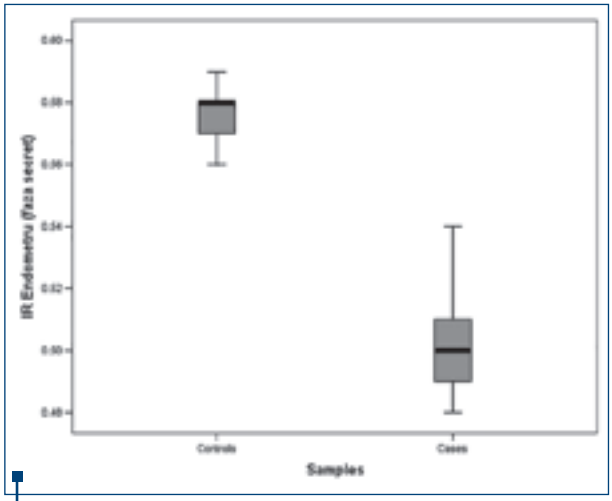

Figure 5. Comparison of arcuate artery resistance in the early secretory phase

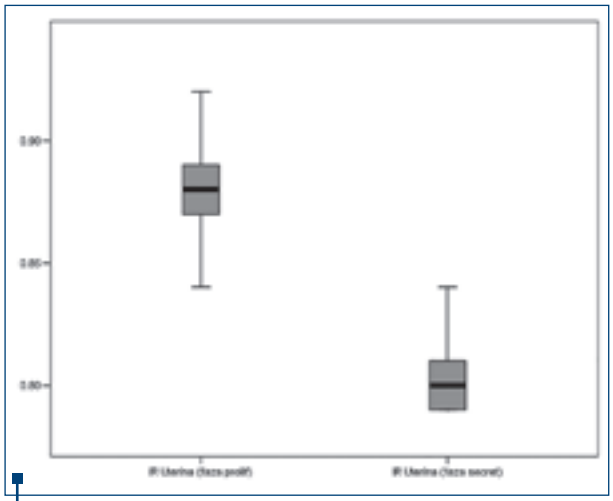

Figure 6. Comparison of uterine artery resistance in the late proliferative phase and in the late secretory phase in patients with ovarian endometrioma

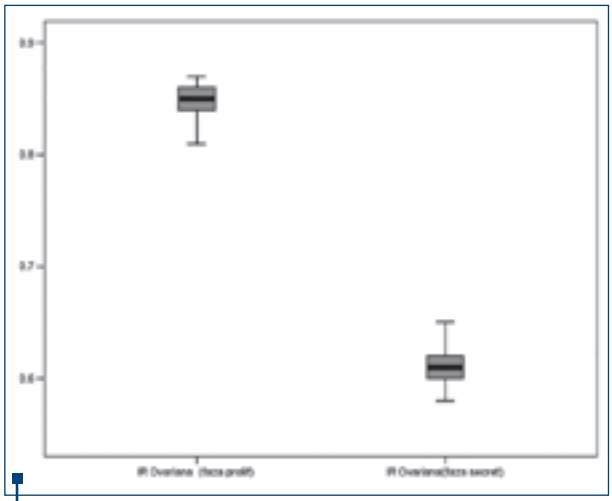

Figure 7. Comparison of ovarian artery resistance in the late proliferative phase and in the late secretory phase in patients with ovarian endometrioma

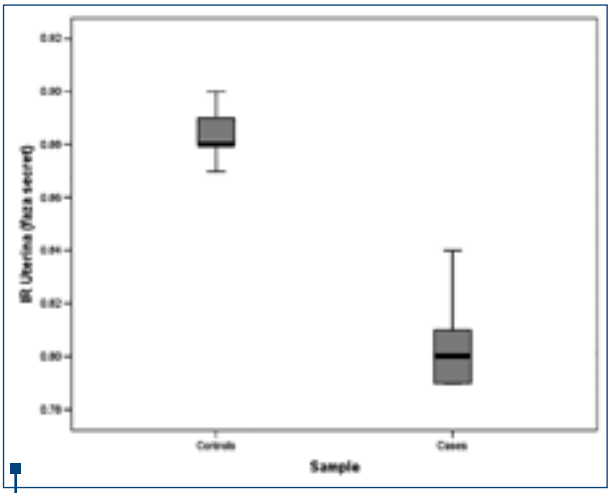

Figure 8. Comparison of ovarian endometrioma wall artery resistance in the late proliferative phase and in the late secretory phase

thout notch, with low resistance, allowing easy differentiation from endometrioma[17].

The ovarian abscess and the pyosalpinx are characterized by an important edematous and inflammatory process causing hypervascularization that can be easily identified by Doppler examination, thus differentiating these entities from endometrioma[18].

In this study, we noted the fact that the RI of uterine arteries significantly changed in patients with ovarian endometrioma, showing a low value compared to the control group. This observation contradicts the idea according to which the pathogenic mechanism of endometriosis-infertility relationship could be represented by abnormalities of uterine artery flow[19].

The alteration of pelvic anatomy caused by the presence of endometriomas and associated inflammation may be responsible for uterine artery flow abnormalities. It is also possible that in the presence of endometrioma associated with blood flow alteration in the uterine

Table 1 The mean differences of the resistance index values between the proliferative phase and the secretory phase for each of the following locations:uterine (0.07±0.03; 95% CI [0.06-0.08]), ovarian (0.24±0.03; 95% CI [0.23-0.25]), endometrial (0.03±0.02; 95% CI [0.03-0.04] and cyst wall arteries (0.19±0.04; 95% CI [0.18-0.21]) are different from 0, the test being statistically significant. In each of these cases, p <0.05 for α = 5% (level of significance)

	Mean differences	Std. deviation of the differences	Std. error of the mean differences	95% confidence interval of the difference		p (Wilcoxon test)
Uterine RI (prolif. phase) - uterine RI (secret. phase)	0.07	0.03	0.00	0.06	0.08	0.00000000000000000004
Ovarian RI (prolif. phase) - ovarian RI (secret. phase)	0.24	0.03	0.00	0.23	0.25	0.0000000000000000000000000000000000000000000000008
Endometrial RI (prolif. phase) - endometrial RI (secret. phase)	0.03	0.02	0.00	0.03	0.04	0.00000000000001
Cyst wall RI (prolif. phase) - cyst wall RI (secret. phase)	0.19	0.04	0.01	0.18	0.21	0.00000000000000000000000000000004

artery may coexist with arteriosclerotic lesions and endothelial dysfunction[20]. This could explain the presence of an increased blood flow in the uterine artery in our study, as the enrolled patients were young patients with low atherosclerotic potential.

The limitations of this study are represented by the relatively small number of cases, by poor intra and interobserver variability, as well as by lack of comparison between endometriosis cyst and other types of cysts.

The association of 3D ultrasound with power Doppler examination provides additional information related to the qualitative aspect of tumor vascularization, through the evidencing of the three-dimensional vascular network, as well as to the quantitative aspect, by means of 3D power Doppler (3D PD) vascular indices.

The arrangement or the density of vessels plays a key role in the evaluation of ovarian tumors. Quantifying blood vessel density during color Doppler evaluation could lead to a wider use in current medical practice, in order to assess pelvic masses than Doppler indices. Our study results are consistent with few other studies. This is one of the first studies that evaluate the vascularization of endometriotic cysts. Thus, further studies are required to confirm our findings.

Conclusions

The vascular pattern of ovarian endometrioma includes peripheral vascularization increased maximum systolic velocity, low blood flow resistance (in the uterine, ovarian, arcuate arteries), the presence of the protodiastolic notch, enhanced vascularization in the late secretory phase. This vascular pattern may contribute to differential diagnosis from other ovarian tumor masses. ■

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